
AMENDMENTS TO THE CLAIMS

Claim 1 (previously presented). A method of screening proteins and polypeptides to identify a protein or polypeptide having a biological activity of interest, which comprises the sequential steps of (i) forming a first library of polynucleotide clones; (ii) expressing an individual protein or polypeptide from each clone in the first library to form a second library of individual proteins and polypeptides therefrom; (iii) assaying the second library to select an individual protein or polypeptide in the second library having a biological activity of interest; and (iv) identifying the protein or polypeptide selected in step (iii) by sequencing the polynucleotide from the first library that encodes the selected protein or polypeptide.

Claim 2 (previously presented). A method as claimed in claim 1 wherein the individual proteins and polypeptides in the second library are assayed for a biological activity selected from the group consisting of an enzymatic protein or polypeptide modification, binding to another molecule, binding to a cell or tissue, and modulating the metabolism of a cell or tissue.

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Claim 3 (previously presented). A method as claimed in claim 2 wherein the first library is a library of cellular mRNA.

Claim 4 (previously presented). A method as claimed in claim 2 wherein the second library of individual proteins and polypeptides comprises fragments of antibody variable regions.

Claim 5 (previously presented). A method as claimed in claim 4 wherein the biological activity of interest is binding to one or more proteins or polypeptides from a cell or tissue.

Claim 6 (withdrawn). A method as claimed in claim 5 wherein any bound proteins or polypeptides from the cell or tissue are themselves screened for enzymatic modification.

Claim 7 (previously presented). A method as claimed in claim 1 wherein the first library of polynucleotide clones is distributed into an array of polynucleotides, and in step (ii) each polynucleotide in the array is then expressed to generate an array of individual proteins and polypeptides.

Claim 8 (previously presented). A method as claimed in claim 7 wherein the array of individual proteins and polypeptides is immobilized onto a solid phase.

Claim 9 (withdrawn). A method as claimed in claim 8 wherein the solid phase is a multi-well plate.

Claim 10 (previously presented). A method as claimed in claim 8 wherein the solid phase is a glass plate and wherein the proteins and polypeptides are immobilized at specific loci on the surface of the plate.

Claim 11 (previously presented). A method as claimed in claim 7 wherein the individual proteins and polypeptides are expressed from the polynucleotides in the first library by *in vitro* transcription and translation.

Claims 12-13 (cancelled).

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Claim 14 (withdrawn). A method as claimed in claim 12 wherein the proteins or polypeptides are indirectly immobilized onto a solid phase through annealing of mRNA in the ribosome display complex to complementary nucleic acid molecules located on the solid phase.

Claim 15 (previously presented). A method for screening proteins and polypeptides to identify a protein or polypeptide having a biological activity of interest, which comprises the sequential steps of:

- (i) generating a first library of polynucleotides in the form of clones selected from the group consisting of DNA molecules, RNA molecules, cell colonies, and plaques;
- (ii) expressing a polynucleotide from each clone in the first library using *in vitro* translation to generate a second library of individual proteins and polypeptides therefrom;
- (iii) dispensing an aliquot of each protein or polypeptide in the second library into a specific locus in a multi-well plate or a solid phase to form a protein and polypeptide array;
- (iv) contacting the array generated in step (iii) with a material selected from the group consisting of a cell extract, a tissue extract, a cell

sample, and a tissue sample;

- (v) assaying each protein and polypeptide in the array to select an individual protein or polypeptide that interacts with the material contacting the array in step (iv), and
- (vi) identifying the individual protein or polypeptide selected in step (v) by sequencing the polynucleotide that encodes the selected protein or polypeptide;

wherein the interaction of the protein or polypeptide with the material contacting the array in step (v) is an interaction selected from the group consisting of modification of a protein or polypeptide in the array, binding of a protein or polypeptide in the array to a molecule from a cell, and binding of a protein or polypeptide in the array to a molecule from a tissue.

Claims 16-25 (cancelled).

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Claim 26 (withdrawn). A method for screening proteins or polypeptides which comprises:

- (i) Generating a gene library in the form of DNA, RNA colonies or plaques;
- (ii) Carrying out *in vitro* translation to produce proteins or polypeptides, wherein the translation reaction includes addition of molecules which bind to mRNA directly or indirectly and facilitate formation of complexes of mRNA, ribosomes and proteins or polypeptides.

Claim 27 (withdrawn). A method for directly selecting a biological phenotype, comprising generating a gene library in the form of DNA, RNA, colonies or plaques; converting the nucleic acid from each clone using *in vitro* translation to generate proteins or polypeptides; followed by bringing one or more of the displayed proteins or polypeptides into association with a target cell to allow binding of one or more proteins or polypeptides to the cell.

Claim 28 (withdrawn). A method as claimed in claim 27 wherein binding to the target cell results in an alteration to the target cell which then permits isolation of the target cell and recovery of genes encoding the displayed protein or polypeptide.

Claim 29 (withdrawn). A method as claimed in claim 27 wherein binding to the target cell results in alteration to the target cell resulting in the production or cessation of production of one or more molecules from the target cell which then permits recovery of genes encoding the displayed protein or polypeptide.

Claim 30 (withdrawn). A method as claimed in claim 29 wherein one or more of the molecules produced by the target cell binds to one or more of the components of the complex.

Claim 31 (withdrawn). A method as claimed in claim 29 wherein one or more of the molecules produced by the target cell is required for the subsequent viability of a living microorganism.

Claim 32 (withdrawn). A method as claimed in claim 31 wherein the microorganism is a bacteriophage or a bacteria.

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Claim 33 (withdrawn). A method as claimed in claim 29 wherein one or more of the molecules produced by the cell is released from the cell and in turn results in the release of other molecules from liposomes.

Claim 34 (withdrawn). A method as claimed in claim 28 wherein the alteration to the cell results in the appearance or disappearance of a cell surface marker on the cell.

Claim 35 (withdrawn). A method as claimed in claim 30 wherein the molecule derived from the target cell is a RNA binding polypeptide such as HIV tat.

Claim 36 (withdrawn). A method as claimed in claim 31 wherein the molecule derived from the target cell is a bacteriophage polypeptide or an antibiotic or a drug resistance enzyme/factor or an essential nutrient.

Claim 37 (withdrawn). A method of screening proteins or polypeptides comprising generating a gene library in the form of DNA, RNA, colonies or plaques; converting the nucleic acid from each clone using *in vitro* translation to generate proteins or polypeptides; followed by bringing one or more of the synthesized proteins or polypeptides into the vicinity of a modified ligand which binds to a receptor on the surface of a cell or tissue to label the synthesized proteins or polypeptides on the cell/tissue surface.

Claim 38 (withdrawn). A method as claimed in claim 37 wherein the displayed proteins or polypeptides are used to isolate cell molecules.

Claim 39 (withdrawn). A method as claimed in claim 37 wherein the ligand is a protein and is modified by attachment to one or more other molecules which can function as all or part of a label or can initiate a labeling reaction.

Claim 40 (withdrawn). A method as claimed in claim 39 wherein phospholipase C is attached to the ligand and liposomes are added after binding of the ligand to the cell or tissue surface such that phospholipase C results in release of the liposome contents.

Claim 41 (withdrawn). A method as claimed in claim 40 wherein the liposome contains streptavidin, HIV tat, signal recognition particle (SRP), an antibody (or fragment thereof), a specific mRNA or protein binding molecule, F pilus or nickel.

Claim 42 (withdrawn). A method as claimed in claim 39 wherein horseradish peroxidase, beta-galactosidase or porin is attached to the ligand.

Claims 43-56 (cancelled).

Claim 57 (withdrawn). An array or library of proteins/polypeptides produced according to a method as defined in claim 15.

Claim 58 (new). The method of claim 1 wherein the first library of polynucleotide clones in step (i) is a library of transformed bacterial cell colonies; the second library of individual proteins and polypeptides is formed by *in vitro* transcription and translation of an individual protein or polypeptide from each bacterial cell colony in step (ii); and the biological activity of interest in step (iii) is post-translational modification of a protein or polypeptide from a tissue extract.

Claim 59 (new). The method of claim 58 wherein the tissue extract is a human brain tissue extract.

Claim 60 (new). The method of claim 58 wherein the post-translational modification is proteolysis.

Claim 61 (new). The method of claim 58 wherein the post-translational modification is phosphorylation.

Claim 62 (new). The method of claim 15 wherein the first library of polynucleotide clones in step (i) is a library of transformed bacterial cell colonies; the protein and polypeptide array is contacted with a tissue extract in step (iii); and in step (iv) the protein and polypeptide array interacts with tissue extract by post-translational modification of a protein or polypeptide from the tissue extract.

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Claim 63 (new). The method of claim 62 wherein the tissue extract is a human brain tissue extract.

Claim 64 (new). The method of claim 62 wherein the post-translational modification is proteolysis.

Claim 65 (new). The method of claim 62 wherein the post-translational modification is phosphorylation.
